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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,660	07/31/2003	Allan C. Spradling	056100-5031	8247

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,660	SPRADLING ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-75* is/are pending in the application.

4a) Of the above claim(s) *49-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendment canceling claims 1-24 and adding new claims 25-75, in the paper of 11/2/2006, is acknowledged. Claims 25-75 are still at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group II, and SEQ ID NO: 1, previous Claims 14, 15 and 18-20 and new claims 25-48, in the paper of 11/2/2006, is acknowledged. It is noted that the election of group II is a change in applicant's previous election of Group I. Since no action on the merits has been issued in the instant application, this change in applicant's election is permitted. In applicant's response, changing applicant's previous election, applicants submit that claims 25-49 are directed to the same invention as previous group II. This is not in fact the case, newly added claim 49 is drawn to a method of modulating chromatin structure in a cell comprising introducing into the cell an agent that alters PARP-e expression, which is the subject matter of previous group I, not group II. As applicants have clearly changed their election from group I to group II, claims 25-48 will be examined.

Applicant's traversal is on the ground(s) that the office action has not met the burden of establishing that Groups II and I are patentably distinct, in particular with respect to establishing a prima facie showing as to the burden of search.

Applicants submit that the method as claimed in Group I cannot be practiced without the nucleic acid of Group II and thus applicants request that Group I be examined with Group II.

Applicants comments regarding the relationship of SEQ ID NO: 1 to SEQ ID NO: 10 are found persuasive and SEQ ID NO: 10 will be considered in addition to SEQ ID NO: 1.

Applicant's complete traversal is acknowledged and has been carefully considered, however is not found persuasive for the reasons previously stated and those repeated herein.

It is noted that previously the claims of group I were drawn to a method of altering the expression of Group II, that is comprising "altering the expression of PARP-e, however newly added claim 49 is drawn to a method of modulating chromatin structure in a cell comprising introducing into the cell an agent that alters PARP-e expression. This is a subgenus of the previous group I, that involves the use of an agent that alters PARP-e expression, which may or may not be a nucleic acid of Group II. Further the method of Group I may be practiced without the polynucleotide of Group II. Thus the methods of Group I continue to be unrelated to the product of Group II.

Applicant's argument is not found persuasive because while the searches for the each of the groups overlap, they are not coextensive. For example, search of Group II would require search of subclass 536/23.2 and search of Group I would require search of subclass 435/69.2. A search of each of this subclass would be unnecessary the search of the elected group II.

Newly added claims 60-75 are drawn to a method of inhibiting the development of an organism, which are different then the claims of newly elected Group II.

This Group of claims is unrelated to the claims of the elected Group II, as the methods of claims 60-75 (Group V) do not use the polynucleotide of Group II or make the polynucleotide of Group II.

The requirement is still deemed proper and is therefore made FINAL.

Claims 49-75 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

There are currently no information disclosure statements in the instant application file.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 (26-48 dependent on) is indefinite in that it is unclear as to the meaning of the recitation "poly (ADP-ribose) polymerase- embryonic". Specifically it is unclear as to the meaning of the term "embryonic" in the phrase and how this differentiates a PARP-e from other PARP molecules. For the purpose of advancing prosecution, "PARP-e" is interpreted as meaning any "PARP" or any molecule having poly (ADP-ribose) polymerase activity.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 31 is directed to all possible nucleic acids comprising at least 15 nucleotides of SEQ ID NO: 1. The specification, however, only provides the representative species of the full length SEQ ID NO: 1, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative

species of these nucleic acids by any identifying functional characteristics or properties, for which no predictability is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 25, 26, 28, 29, 31, 33-39 and 41-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule encoding a poly (ADP-ribose) polymerase consisting of SEQ ID NO: 1, does not reasonably provide enablement for any nucleic acid comprising a mere 15 nucleotides of SEQ ID NO: 1 or having a mere 70% identity to SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 25, 26, 28, 29, 31, 33-39, 41-48 are so broad as to encompass any nucleic acid comprising a mere 15 nucleotides of SEQ ID NO: 1 or having a mere 70% identity to SEQ ID NO: 1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acids broadly encompassed by the claims, including any nucleic acid comprising a mere 15 nucleotides of SEQ ID NO: 1. The claims rejected under this section of U.S.C. 112, first paragraph, place minor structural limits on the claimed molecules. Since the amino acid sequence of a protein (and thus the encoding nucleic acid sequence) determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to those nucleic acids consisting of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any nucleic acid comprising a mere 15 nucleotides of SEQ ID NO: 1 or having a mere 70% identity to SEQ ID NO: 1, because the specification does not establish: (A) regions of the nucleic acid structure which may be modified without effecting poly(ADP-ribose) polymerase activity; (B) the general tolerance of poly(ADP-ribose) polymerase encoding nucleic acids to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a poly(ADP-ribose) polymerase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the poly(ADP-ribose) polymerase or desired activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those nucleic acids of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of modifications of any of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those nucleic acids having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25, 28, 31, 33, 34, 35, 37, 38, 41, 42, 46, 47, are rejected under 35 U.S.C. 102(b) as being anticipated by Uchida et al. (Proc. Natl. Acad. Sci. USA, Vol 90, pages 3481-3485, May 1993).

Uchida et al. teach the cloning of cDNA encoding Drosophila poly(ADP-ribose) polymerase. Uchida et al. specifically teach an isolated nucleic acid encoding a PARP-e comprising a nucleotide sequence at least 70% identical to SEQ ID NO: 1(see Figure 1 and supporting text). Uchida et al. further teach that said nucleic acid comprise at least 15 nucleotides of SEQ ID NO: 1, and hybridizes to SEQ ID NO: 1. Uchida et al.

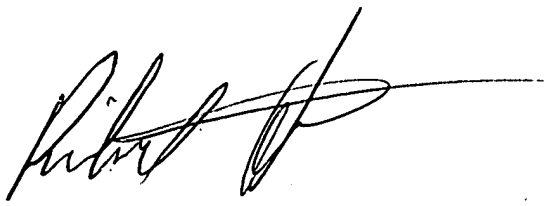
further teach the nucleic acid that is complementary to SEQ ID NO: 1 by virtue of the cloning of said nucleotide sequence into pBluescript KS- as well as vectors and prokaryotic host cells comprising said nucleic acid.

Thus Uchida et al. anticipates claims 25, 28, 31, 33, 34, 35, 37, 38, 41, 42, 46, 47.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
1/11/2007